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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

ATTACHMENT TO ADVISORY ACTION

5. CONT.

Applicant's amendment to the specification places the application in compliance with 37 CFR 1.821-1.825.

The amendment to the specification has also removed the new matter added with the 3/6/07 amendment. The objection under 35 U.S.C. 132(a) is therefore withdrawn.

The rejection of claims 7-8 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendments to claim 7.

11. CONT.

Applicant's amendments to the claims and arguments have been fully considered but not found persuasive in overcoming the following rejections for reason of record as discussed in detail below.

The rejection of the pending claims under 35 USC 112, first paragraph, for lack of written description, is maintained in part. Applicant's cancellation of claim 9 overcomes the rejection based on lack of written description for siRNA related to a therapeutic drug or prodrug. Regarding the lack of written description concerning the genus of full length primate Hpr, applicant argues that Lugli et al., referred to the previous response but not submitted, and newly submitted references of McEvoy, Erickson, Shuey, Heidenreich, and Martinez demonstrate that full length Hpr is present in a very limited number of species such that the sequences disclosed in the specification are representative of the genus. This is not agreed. Lugli et al. is still not of record. Further, the previous office action pointed out that as a post-filing reference, Lugli, if submitted, cannot be relied upon for teaching the state of the art at the time of filing. Heidenreich et al., Shuey et al., and Martinez et al. teach siRNA and RNAi, and provide no teachings or guidance regarding primate Hpr genes. McEvoy et al. teaches the cloning of chimpanzee Hpr, but agrees with the teachings of Smith et al., previously cited by the examiner, that this gene is a non-functional pseudogene due to a frameshift mutation. Erickson et al. teaches partial sequencing of the rhesus monkey Hpr, but discloses on page 586 that this gene, like the chimpanzee Hpr, is a pseudogene with a frameshift mutation. Thus, none of these references

provides any evidence that genes encoding full length Hpr were known or available in the prior art at the time of filing in primates other than humans. Further, applicant's argument that there are only three members of this genus is based on upon knowledge acquired after the filing date of the instant application. There is simply no evidence of record that the size of the genus of full length primate Hpr was known as of 2002, the effective filing date. Therefore, the rejection of record is maintained.

The rejection of the pending claims under 35 USC 112, first paragraph, for lack of enablement is maintained. As noted above, applicant's evidence for description of species of full length primate Hpr other than human Hpr is post-filing and does not represent the state of the art as of the effective filing date of this application. Second, applicant's argument that the statement of page 237 of Shinamura shows that lysosomal targeting of Hpr had been established in the prior art does not overcome the rejection of record. The issue is not whether Hpr can be targeted to the lysosome, the issue is whether Hpr, when present in the lysosome, can in fact lyse all species of Trypanosome. The previous office action stated that Shinamura et al., while suggesting that the lack of lysis of *Trypanosoma brucei rhodensiense* "may" be due to reduced endocytosis and failure to enter the lysosome, does not teach that the exact reason for the failure of TLF-1 containing Hpr to lyses *Trypanosoma brucei rhodensiense* had been determined. Neither Shimamura et al. nor the instant specification demonstrates that improving intracellular targeting of Hpr to the lysosome would in fact result in lysis of *Trypanosoma brucei rhodensiense.* Thus, applicant's argument does not overcome the lack of enabling disclosure for lysing any Trypanosome, including any subspecies of *Trypanosoma brucei,* by introducing a gene encoding Hpr and a lysosomal targeting sequence. Finally, newly submitted references, Anzar, Kunisawa, Nakanishi and US Patent 4,356,167, do not overcome the lack of enablement for delivering therapeutic levels of a drug by administering a trypanosome comprising a drug or prodrug. It is noted that the previous office action stated that the claims are not limited to liposomally packaged drugs, and that the only guidance relevant to drug delivery provided by the specification occurs on page 18, which states that, "Non-nucleic acid therapeutic agents are packaged in a sacromastigophoric organism through electroporation or phagocytosis of liposomally packaged therapeutic agents". Neither the specification nor prior art of record teaches that drugs, either packaged in a liposome or not, can be stably maintained in a

Trypanosome, or subsequently release to a host organism upon lysis of the Trypanosome. None of the submitted references overcomes these issues. Kunisawa et al. and Nakanishi et al. teach Sendai virus based fusogenic liposomes for delivering drugs or antigens into the cytoplasm of mammalian cells, and provide no teaching or suggestion that such fusogenic liposomes can introduce a drug into a Trypanosome. Anzar et al. teaches the delivery of fluorescent molecules to sperm using liposomes. Again, there is no teaching or suggestion regarding packaging liposomes in Trypanosomes. Finally, US Patent 4,356,167 teaches liposomes for oral or parenteral administration. This patent provides no teachings regarding uptake of the liposomes by cells of any kind. In addition, applicant's statement that this patent in example 6 teaches that liposomes once subjected to endocytosis were stable for 48 hours is incorrect. Example 6 states that, "liposomes were stable after 48 hours dialysis against distilled water". There is simply no teaching whatsoever in the 4,356,167 patent about endocytosis of liposomes. As such, the submitted references are not persuasive in overcoming the rejection of record.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633